AstraZeneca

December 30, 2004

Dockets Management Branch
(HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 2004D-0440
Response to FDA Call for Comments
Draft Guidance for Industry on Computerized Systems Used in Clinical Trials

Dear Sir or Madam:

Reference is made to the October 4, 2004 Federal Register notice announcing the request for comments on the draft "**Guidance for Industry: Computerized Systems Used in Clinical Trials.**"

AstraZeneca has reviewed this Draft Guidance and our comments are attached.

Please direct any questions or requests for additional information to me, or in my absence, to Tony E. Catka, Associate Director, USRA, Regulatory Project Management, at 302-885-9659.

Sincerely,

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Director,
USRA, Regulatory Project Management
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Enclosure

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Draft Guidance
Docket No. 2004D-0440, Draft Guidance for Industry on Computerized Systems Used in Clinical Trials

General Comments

Comment 1

It is recommended that the term "site" be clarified. It is ambiguous at times as to whether site means investigation site, sponsor site, or vendor site, etc.

Page Number	Section Number	Comment or proposed replacement text
3	Intro 60-61	Computerized medical devices were excluded from this document. Is a document which gives guidance on these devices forthcoming?
4-5	General	It appears that there is no longer a recommendation that e-CRFs and e-diaries should be designed to allow users to make annotations? While this is probably not necessary for e-diaries, this could result in potential loss of data quality with respect to e-CRFs.
4, 8	General III.2, 78-81 VIII B, 264	It is suggested that the high expectation for documentation availability at clinical trial investigator sites relating to the implementation of systems may be unnecessarily burdensome.
4	III 76-77	For Principle 1 the following additional language is recommended: *'Any significant changes to a computerized system used to create, modify etc. should be documented in the study records."*
4	III 78-81	For Principle 2 the following additional language is recommended *'Any significant changes to the hardware and software should be documented in the study records."*
4	III 78-81	A reference to the retention of the documentation of the hardware is made. However as the hardware could change quite frequently, it could be difficult to regularly update this documentation. Many times the sponsors are not informed of the changes. Is it correct to assume that it is only necessary to keep the initial hardware documentation?
4	III 78-81	Clarification is requested regarding the extent to which system configuration changes need to be documented at the study level. For example, configuration management documentation on data management systems that service multiple studies must be maintained at the system level. It is not feasible to duplicate it for every study.

Page Number	Section Number	Comment or proposed replacement text
4	III 92	This is a specific example of the general comment above: In line 92 "Source document at the site" is mentioned but it is unclear as to what site is being specified, Does it mean the center, at the Marketing Company or at the R&D site?
4, 7, 12	III 105, VI B 206, X 453, XI 461	Clarification is needed for the word "firms"; From the context it is not clear as to whether this applies to investigators or sponsors.
4 and 7	III 107- 109 (Also VI B 213-215)	Is the reason for a change a required audit trail component for all record modifications? To be in line with ICH GCP (4.9.3 and 5.18.4 (n)), it is suggested that the statement read as follows: "We recommend that audit trails or other security methods used to capture electronic record activities document who made the changes, when and, ***if necessary***, why changes were made to the electronic record."
5	V 137-146	The recommendation that an SOP describing "Alternative Recording Methods" in case of system unavailability, be available at investigator sites is a welcomed improvement.
5	V 137-146	Does the term **site** in this section refer specifically to an investigator site? If so, some of the SOPs seem impractical and inappropriate to be kept at each investigator site. However, some SOPs for computerized system use are missing from this list if the recommendation refers to sponsor or vendor sites. For example, when dealing with some sponsor or vendor-supplied computerized systems and services such as IVRS or web-based systems, the supplier would be responsible for such activities as installation, maintenance, help desk/Tech Support, and data backup. This section would benefit from some qualification as it currently reads as though SOPs covering all the topics listed should always be available at the investigator site. Need clarification if SOPs would be needed even if the system is installed elsewhere and accessed remotely.
5	V 146	It is recommend that 'Archiving or Decommissioning' is added as bullet 8.
5	VI A 151	It is recommended that Section 'A. Computer Access Controls' require systems to record/log attempts at unauthorized access.
5	VI A 151-172	It appears that there is no longer a requirement for the name of the person performing data entry/modification to appear on the screen. The displayed name on the screen is a confirmation that the correct person was logged on to the system and that their name was then entered into the audit trail. This is a useful deterrent to accidentally using someone else's account or intentional falsification, especially in a hospital setting where handwritten/electronic signature equivalence is not yet part of the culture.
7	VI B 214	It is recommended that the words "what changes" be inserted into this line" so that it reads as follows: *"document what changes were made, who made*

Page Number	Section Number	Comment or proposed replacement text
		them, when and why the changes were made to the electronic record". In some cases the "why" may not be so easy to capture.
7	VI C 233	It appears that the requirement for Date/Time Stamps' is a more stringent requirement now for GCP than for the GMP, GLP codes. This is no longer a requirement of the revised Part 11 Guidance for ER/ES. It is recommended that only the requirements of the predicate GCP rule be applied, and that (C) is removed or appropriately modified to meet GCP requirements.
8	VII A 258 – 9	The current draft guidance recommends against the use of features that automatically enter data into a field when the field is bypassed. However this broad recommendation may need reexamination. It is noted that such features can be extremely useful in generating derived data e.g. time interval between two dates or internal references such as linking a study to a project. Such features increase efficiency and reduce errors.
8	VII.B 263	As written this section requires documentation that fully describes and explains how data were obtained and managed and how e-records were used to capture data. Including this in protocols could be quite burdensome and therefore it is recommended that this be deleted. This general information is already mentioned in a more sensible approach in Section III.2.
9	VIII 304-305	The restrictions on use of external applications to browse, query or report seem too far-reaching and it is recommended that they be lifted. These restrictions could be a major issue when archiving is considered. However it is agreed that procedures or controls are needed to prevent such applications from altering data.
9	VIII 307-309	It is unclear as to what "accessible at the site" means. The requirements described here are highly burdensome to be maintained at the investigator site when the information applies to sponsors. If this means kept at the site, is it reasonable (or even feasible) to expect any one site to retain the complete and current cumulative record of authorized personnel and their access privileges for the entire study? Or does this section refer to a cumulative record of personnel just for a particular site?
9	VIII 311-317	Care needs to be taken to ensure that this may not be misinterpreted to mean that each system has to own its own hardware.
9	IX 329-331	It is unclear in this section as to whether all system documentation relating to its development and validation should be available at sites where clinical trials are conducted. If this is indeed the case this requirement is not really feasible, as much of this documentation will reside with the vendor in the case of vendor-supplied documentation, or at some central archiving location on the part of the sponsor. If it instead means that a system description should be readily available – this is feasible. It could be inferred from lines 350-354 that development and validation documentation would not be included in the term 'systems documentation'. A definition of what is covered by the term "systems documentation" would be useful.
11	IX B	It is noted that it may not always be practical or possible to have all

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	388	necessary records held permanently for the design level vendor validation.
11	IX C 413	Regarding change controls: If a system version is changed at a global level, would it be necessary to document the change at all levels in all the countries?
15	Definitions 541-542	In the definition of "Certified Copy" it is not clear whether the verification of a copy of original information 'as indicated by dated signature' refers to the signature being that of the *original* signer where the original information was a wet-ink signed document. If this is not the case, the verification process is open to fraud if photocopying, microfilming, and microfiching. If the copy is in electronic format, does the dated signature then have to be an e-signature compliant with Part 11?